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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/049,986 | 07/01/2002 | Seishi Nagamori | 56972 (71526) | 2684 |
| 21874 | 7590 | 08/24/2006 | EXAMINER | |
| EDWARDS & ANGELL, LLP | | | HORNING, MICHELLE S | |
| P.O. BOX 55874 | | | ART UNIT | |
| BOSTON, MA 02205 | | | PAPER NUMBER | |
| | | | 1648 | |

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/049,986

Applicant(s)

NAGAMORI, SEISHI

Examiner

Michelle Horning

Art Unit

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 November 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-29 is/are pending in the application.
- 4a) Of the above claim(s) 1-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21-28 ²⁵ are rejected.
- 7) ☒ Claim(s) 29 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This office action is in response to communication filed 11/03/2005. Please note that this application has been transferred to another examiner and all correspondences regarding this application should be directed to Michelle Horning. The status of the claims is as follows: claims 1-20 have been cancelled and claims 21-29 are under current examination.

In view of Applicant's amendments and persuasive arguments, the following objections and rejections have been withdrawn:

1. objection to the specification;
2. objection to the drawings;
3. 35 USC 112, second paragraph; and
4. 35 USC 103.

The objection to the specification has been withdrawn following Applicant's amendment. Applicant has provided an amendment cross-noting the international application upon which this application's priority is based. The amendment provides both the international application number and the international filing.

The objection to the drawings was an incorrect objection. It is noted that the Applicant has provided the Office with courtesy copies of drawings containing numbers and characters in English. This objection is withdrawn.

In view of the revisions to the claims, all 35 USC 112, second paragraph rejections have been withdrawn.

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Applicant's arguments regarding claim rejections under 35 USC 103 were considered and found to be partially persuasive. Briefly, none of the references cited in the previous 892 form are drawn to a method of viral proliferation of cells under continuously circulating medium. Further, no combination of the disclosures from the mentioned references would overcome this limitation. Thus, this rejection is withdrawn.

New Claim Rejections

35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 29 is dependent on cancelled claims 1 and 7.

35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 21-26 and 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent Application 11/097,994 in view of Carloni et al (1993).

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The instant application is drawn to a method for proliferating a hepatitis C virus, characterized by immobilizing human hepatocytes, preferably FLC-4 cells, onto a porous carrier. This carrier is housed within a culture vessel, more specifically a radial flow bioreactor, in which there is a continuous stream of liquid culture medium.

Following immobilization of the hepatocytes, the cells are infected with the hepatitis C virus. Further, the hepatitis C virus is proliferated within a continuous stream of liquid culture medium in which this medium may be recycled or fresh medium.

The invention of US Patent Application 11/097,994 is drawn to a similar method for propagating SF-9 or other cells, including mammalian cells, which are infected with virus for proliferation (see paragraph 91). This application discloses a method comprising a bioreactor for cell culture, a vessel for culture medium and a means for culture medium circulation (see Figure 1 for bioreactor apparatus and Figure 4 for radial flow bioreactor). Cells are attached or immobilized to a semipermeable membrane, including a hollow fiber filter or porous hollow microballoons housed within the bioreactor (see paragraphs 27 and 28). Attached cells are then infected by virus "prior, during or after growth" (see paragraph 109). Of note, during growth suggests that the cells are in a continuous stream of liquid medium after infection (see paragraph 100). Further, the apparatus to which this method is drawn to can be modified to provide the cells with either new or recycled medium (see Medium Replenishment Loop 200 in Figure 1 and paragraph 120 describing the valve system).

Although this prior art reference is not specifically drawn to proliferation of hepatitis C virus in hepatocytes, it is drawn to virus propagation (see Example 3 for

proliferating viral influenza) in infected cells. Further, this reference discloses the means in which pH, temperature, oxygen concentration and carbon dioxide concentration may be altered to provide optimal conditions for virus propagation in mammalian cells (paragraph 8). While this reference does not specifically disclose the optimal conditions required for hepatitis C virus in human hepatocytes or in an established hepatocyte cell line, this knowledge is well known in the art and is disclosed by Carloni et al (1993). The conditions, including the concentration of CO₂, are provided in Methods. Further, Carloni et al discloses the development of a cell culture system of human fetal hepatocytes that is susceptible to hepatitis C virus (see abstract). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of US Patent Application 11/097,994 as taught by Carloni et al. The skilled artisan would have been motivated to do so to provide a means of amplifying hepatitis C virus for further study. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 23 and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent Application 11/097,994 in view of Akoi et (1998).

These claims are drawn to a method that utilizes an established human cell line, specifically, the FLC-4 cell line. While US Patent Application 11/097,994 does not disclose this specific cell line, the prior art reference by Akoi et al meets this limitation by teaching the use of the FLC-4 cell line for the successful infection of hepatitis C virus. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of US Patent Application 11/097,994 as

taught by Akoi et al. The skilled artisan would have been motivated to do so because Akoi et al disclose that FLC-4 cells can be successfully infected with hepatitis C virus, further leading to an increase in stability and translational efficiency of HCV RNA (see Discussion). Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

CONCLUSION

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michelle Horning whose telephone number is 571-272-9036. The examiner can normally be reached on Monday-Friday, 8:30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 570-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for unpublished application is available through Private PAIR only. For more information about PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Michelle Horning
Patent Examiner


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